

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Simon F. Williams, David P. Martin, and Frank A. Skraly

Serial No.: Divisional of 09/535,146

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For: MEDICAL DEVICES AND APPLICATIONS OF
POLYHYDROXYALKANOATE POLYMERS

Box Patent Application
Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to examination, please amend the application as follows.

In the Specification

On page 1, line 5, please delete "Priority is claimed", and insert --This application is a divisional of pending prior application U.S. Serial No. 09/535,146 filed March 24, 2000, which claims priority-- in place thereof.

In the Claims

1. (amended) The device of claim 30 wherein the [A] biodegradable polyhydroxyalkanoate composition [that] has a controlled degradation rate of less than two years[, preferably less than one year,] under physiological conditions, wherein the degradation rates of the polyhydroxyalkanoates are manipulated through addition of components to the polymeric composition, selection of the chemical composition, molecular weight, processing conditions, or form of the composition.
2. (amended) The [composition] device of claim 1 wherein the chemical composition of the polyhydroxyalkanoate is altered through selection of monomers which are incorporated into the polymer, by alteration of the linkages, chemical backbone or pendant groups, or by manipulation of the molecular weight.
3. (amended) The [composition] device of claim 1 wherein the polyhydroxyalkanoate composition comprises additive altering the degradation rate of the composition, wherein the additives are selected from the group consisting of hydrophilic substances, hydrophobic substances, and coating which alter water uptake by the composition.
4. (amended) The [composition] device of claim 1 wherein the polyhydroxyalkanoate comprises a polymer selected from the group of consisting of poly-4-hydroxybutyrate, poly-4-hydroxybutyrate-co-3-hydroxybutyrate, poly-4-hydroxybutyrate-co-2-hydroxybutyrate, and copolymers and blends thereof.

5. (amended) The [composition] device of claim 1 wherein the polyhydroxyalkanoate comprises a polymer selected from the group consisting of poly-3-hydroxybutyrate-co-3-hydroxyhexanoate, poly-3-hydroxybutyrate-co-3-hydroxyoctanoate, poly-3-hydroxybutyrate-co-3-hydroxydecanoate, and copolymers and blends thereof.

6. (amended) The [composition] device of claim 1 wherein the polyhydroxyalkanoate comprises one or more units which alter the chemical stability of the polymer backbone.

7. (amended) The [composition] device of claim 1 comprising unit(s) promoting chain scission.

8. (amended) The [composition] device of claim 7 wherein the units contain more than two functional groups.

9. (amended) The [composition] device of claim 1 wherein a heteroatom is incorporated into the polymer backbone chain.

10. (amended) The [composition] device of claim 9 wherein the heteroatom is selected from the group consisting of oxygen, sulfur or nitrogen.

11. (amended) The [composition] device of claim 7 wherein the units are incorporated into the polymer backbone with chemical linkages selected from the group consisting of ester, amide, ether, carbamate, anhydride, and carbonate.

12. (amended) The [composition] device of claim 11 wherein the units are selected from the group consisting of 2-hydroxyacids, 2-hydroxyalkoxyacetic acids, amino acids, amino alcohols, diacids, triols, and tetraols.

13. (amended) The [composition] device of claim 12 wherein the 2-hydroxyacids are 2-hydroxyalkanoic acids.

14. (amended) The [composition] device of claim 13 wherein the 2-hydroxyalkanoic acid is lactic acid or glycolic acid.

15. (amended) The [composition] device of claim 12 wherein the 2-hydroxyacids are 2-hydroxyalkenoic acids.

16. (amended) The [composition] device of claim 12 wherein the 2-hydroxyalkoxyacetic acids are selected from the group consisting of 2-hydroxyethoxy acetic acid and 3-hydroxypropoxy acetic acid.

17. (amended) The [composition] device of claim 1 wherein the polymer comprises pendant groups that catalyze the degradation of the polymer backbone.

18. (amended) The [composition] device of claim 17 wherein the pendant groups are selected from acidic and basic groups.

19. (amended) The [composition] device of claim 17 comprising reactant pendant groups that cause polymer chain scission.

20. (amended) The [composition] device of claim 19 wherein the reactant pendant groups are selected from nucleophiles and electrophiles.

21. (amended) The [composition] device of claim 17 wherein the pendant groups are selected from the group consisting of alcohols, acids, and amine groups.

22. (amended) The [composition] device of claim 1 comprising additives altering the chemical stability of the polyhydroxyalkanoate.

23. (amended) The [composition] device of claim 22 wherein the additives promote chain scission.

24. (amended) The [composition] device of claim 22 wherein the additives are selected from the group consisting of acids, bases, electrophiles, nucleophiles, plasticizers, polymers, pore forming agents, and agents designed to reduce the polymer crystallinity.

25. (amended) The [composition] device of claim 1 comprising pore forming agents.

26. (amended) The [composition] device of claim 25 wherein the pore forming agents are lyophilizable particles.

27. (amended) The [composition] device of claim 25 wherein the pore forming agents absorb water.

28. (amended) The [composition] device of claim 1 further comprising one or more active agents.

29. (amended) The [composition] device of claim 28 wherein the active agent is selected from the group consisting of growth factors, alginates, silver salts, antiseptics, analgesics, and preservatives.

30. A device comprising a biodegradable polyhydroxyalkanoate composition that has a controlled degradation rate of less than two years, preferably less than one year, under physiological conditions,

wherein the degradation rates of the polyhydroxyalkanoates are manipulated through addition of components to the polymeric composition, selection of the chemical composition, molecular weight, processing conditions, or form of the composition, as defined by any of claims 1-29,

wherein the device is selected from the group consisting of sutures, suture fasteners, meniscus repair devices, rivets, tacks, staples, screws, bone plates and bone plating systems, surgical mesh, repair patches, slings, cardiovascular patches, orthopedic pins, adhesion barriers, stents, guided tissue repair/regeneration devices, articular cartilage repair devices, nerve guides, tendon repair devices, atrial septal defect repair devices, pericardial patches, bulking and filling agents, vein valves, bone marrow scaffolds, meniscus regeneration devices, ligament and tendon grafts, ocular cell implants, spinal fusion cages, skin substitutes, dural substitutes, bone graft substitutes, bone dowels, wound dressings, and hemostats.

31. (amended) A method for making a device that has a controlled degradation rate of less than two years, more preferably less than one year under physiological conditions, comprising

providing comprising a biocompatible polyhydroxyalkanoate composition, as defined by [any of claims 1-29] claim 1, and

forming or incorporating the polyhydroxyalkanoate composition into a device selected from the group consisting of sutures, suture fasteners, meniscus repair devices, rivets, tacks, staples, screws, bone plates and bone plating systems, surgical mesh, repair patches, slings,

cardiovascular patches, orthopedic pins, adhesion barriers, stents, guided tissue repair/regeneration devices, articular cartilage repair devices, nerve guides, tendon repair devices, atrial septal defect repair devices, pericardial patches, bulking and filling agents, ligament and tendon grafts, ocular cell implants, spinal fusion cages, skin substitutes, dural substitutes, bone graft substitutes, bone dowels, heart valves and vascular grafts, wound dressings, and hemostats.

32. The method of claim 31 wherein the processing forming or incorporating process is selected from the group consisting of solvent casting, melt processing, fiber processing, fiber spinning, fiber weaving, extrusion, injection molding, compression molding, lamination, and microparticle formation.

33. The method of claim 31 further comprising incorporating an active agent into the polyhydroxyalkanoate.

Please cancel claim 34.

Remarks

This divisional application is filed in response to the restriction requirement mailed June 26, 2001, in prior application U.S. Serial No. 09/535,146.

A marked-up copy and a clean copy of page 1 of the specification are enclosed. A copy of the claims as pending is attached to this Preliminary Amendment as "Appendix I".

Divisional of U.S.S.N. 09/535,146
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Respectfully submitted,



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CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this paper and any documents referred to as attached or enclosed are being deposited with the United States Postal Service on this date, February 26, 2002, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Express Mail Label No. EL 639 985 126 US, addressed to Box Patent Application, Commissioner of Patents and Trademarks, Washington, D.C. 20231.



Pam Turnbough

Date: February 26, 2002

**Marked-up Copy of Amended Specification Pages
Pursuant to 37 C.F.R. § 1.121(b)(1)(iii)**

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MEDICAL DEVICES AND APPLICATIONS OF POLYHYDROXYALKANOATE POLYMERS

Cross-Reference To Related Applications

5 [Priority is claimed] This application is a divisional of pending prior application U.S. Serial No. 09/535,146 filed March 24, 2000, which claims priority to U.S. Serial No. 60/142,238, filed July 2, 1999, and U.S. Serial No. 60/126,180, filed March 25, 1999.

Field of the Invention

10 The present invention generally relates to polyhydroxyalkanoate ("PHA") biopolymers and medical uses and application of these materials.

Background of the Invention

In the medical area, a number of degradable polymers have been developed that break down *in vivo* into their respective monomers within weeks
15 or a few months. Despite the availability of these synthetic degradable polymers, there is still a need to develop degradable polymers which can further extend the range of available properties, particularly mechanical properties.

Polyhydroxyalkanoates are natural, thermoplastic polyesters and can be processed by traditional polymer techniques for use in an enormous variety of
20 applications, including consumer packaging, disposable diaper linings and garbage bags, food and medical products. Initial efforts focused on molding applications, in particular for consumer packaging items such as bottles, cosmetic containers, pens, and golf tees. U.S. Patent Nos. 4,826,493 and 4,880,592 describe the manufacture of poly-(R)-3-hydroxybutyrate ("PHB") and
25 poly-(R)-3-hydroxybutyrate-co-(R)-3-hydroxyvalerate ("PHBV") films and their use as diaper backsheet. U.S. Patent No. 5,292,860 describes the manufacture of the PHA copolymer poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) and the use of these polymers for making diaper backsheet film and other disposable items. Diaper back sheet materials and other materials for manufacturing
30 biodegradable or compostable personal hygiene articles from PHB copolymers other than PHBV are described in PCT WO 95/20614, WO 95/20621, WO

**Clean Copy of Amended Specification Pages
Pursuant to 37 C.F.R. § 1.121(b)(1)(ii)**

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